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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of: Curtis, Rory A.J.

Serial No.: 09/587,111

Filed: June 2, 2000

For: NOVEL MEMBERS OF THE
CAPSAICIN/VANILLOID RECEPTOR FAMILY OF
PROTEINS AND USES THEREOF

Attorney Docket No.: MNI-062CP2DV1

Group Art Unit: 1646

Examiner: Ulm, J. D.

Commissioner for Patents

Box AF

Washington, D.C. 20231

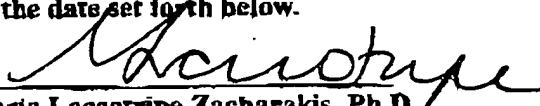
Certificate of Facsimile Transmission

I hereby certify that this correspondence is being facsimile transmitted to the Commissioner for Patents,
Box AF, Washington, D.C. 20231 on the date set forth below.

By:

4/11/03

Date of Signature


Maria Laccorripe Zacharakis, Ph.D.

Attorney for Applicant

Limited Recognition Under 37 C.F.R. 10.9(b)

DECLARATION PURSUANT TO 37 CFR §1.131

Dear Sir:

I, Rory A.J. Curtis, a citizen of the United Kingdom, residing at 78 Hardwick Road,

Ashland, Massachusetts 01721 hereby declare as follows:

Serial Number: 09/587,111

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Group Art Unit: 1646

(1) I am the inventor of the subject matter described and claimed in the above-identified application.

(2) Prior to January 22, 1999, the invention described and claimed in the above-referenced patent application was completed in this country, as evidenced by the following:

(a) Prior to January 22, 1999 I had completed the sequencing of the full length human VR-2 (SEQ ID NO:5) as evidenced by copies of the assembled contig map and the complete sequence of SEQ ID NO:5 derived from the contig map. The contig map and sequence print-out are submitted herewith as Exhibits A and B, respectively.

(b) Prior to January 22, 1999 I had determined that the polypeptide of SEQ ID NO:5 was a vanilloid receptor based on the results of a blast search using the amino acid sequence of SEQ ID NO:5. The top hit in this blast search analysis is rat vanilloid receptor 1 (VR-1; accession number AF029310). Based on the percent identity and percent similarity between the polypeptide of SEQ ID NO:5 and rat VR-1, and the fact that rat VR-1 was the top hit in the blast search analysis I determined that the polypeptide of SEQ ID NO:5 was a vanilloid receptor. The results of the blast search analysis are submitted herewith as Exhibit C.

(c) Prior to January 22, 1999, I had determined that the polypeptide of SEQ ID NO:5 represents a unique target for pain and that it may be responsible for hypersensitivity in chronic neuropathic pain, as evidenced by a copy of the "Qualified Target Summary Sheet" generated for this molecule. The Qualified Target Summary Sheet is submitted herewith as Exhibit D.

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(d) According to my routine practice, immediately after identifying the polypeptide of SEQ ID NO:5 as a vanilloid receptor (hVR-2) associated with pain and classifying it as a Qualified Target, I contemplated routine uses of this molecule such as: (i) use of the molecule in screening assays to identify modulators of the vanilloid receptor or (ii) use of this molecule in the diagnosis of conditions/diseases associated with, for example, aberrant vanilloid receptor (hVR-2) nucleic acid expression or activity, e.g., pain disorders, as evidenced by a copy of the "Qualified Target Summary Sheet" generated for this molecule.

(e) The dates deleted from the contig map (Exhibit A), the sequence print-out (Exhibit B), the blast search results (Exhibit C), and the Qualified Target Summary (Exhibit D) are prior to January 22, 1999.

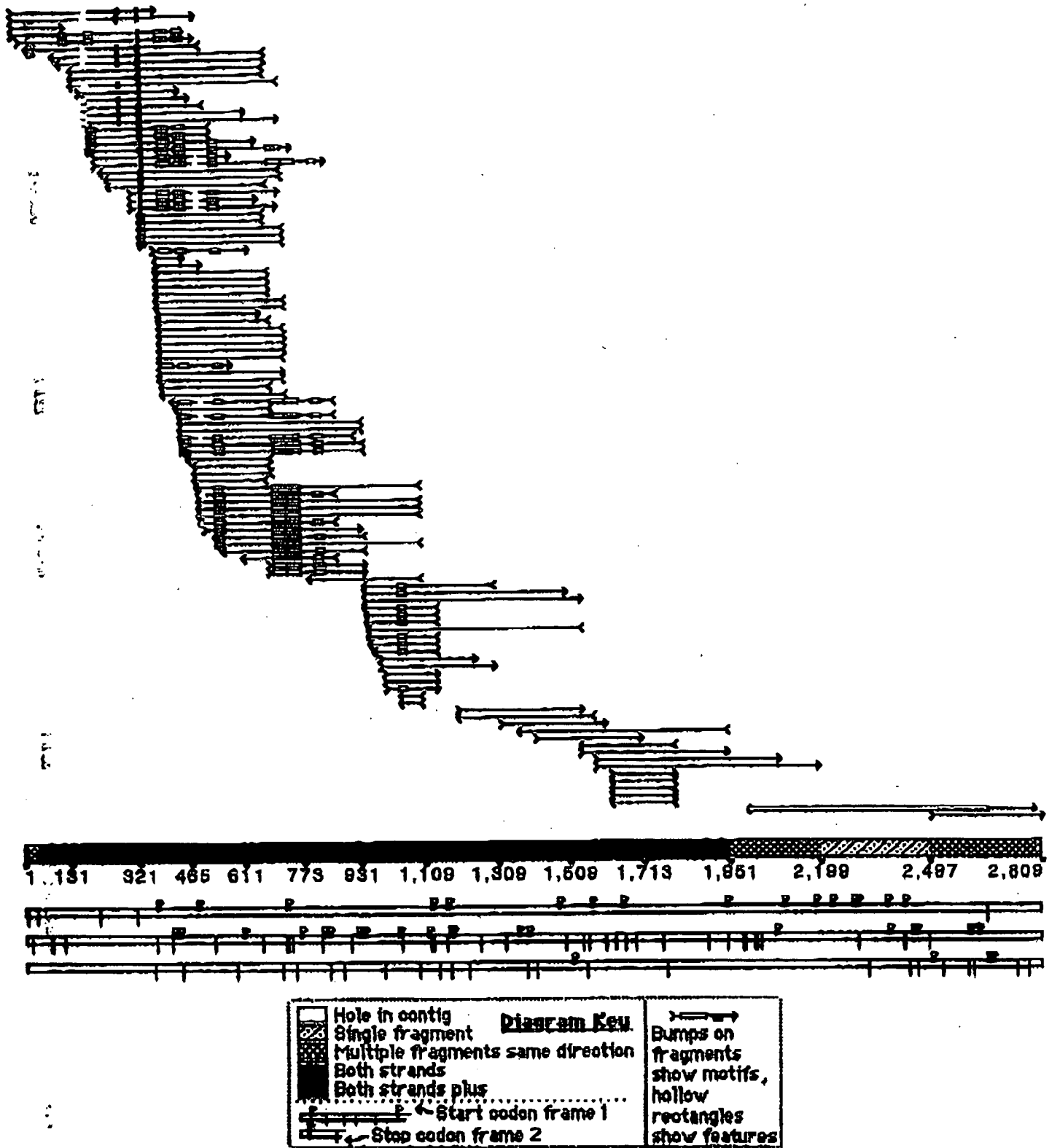
I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this Application for Patent or any patent issuing thereon.

Rory Curtis
Rory A.J. Curtis, Ph.D.

4/10/2003
Date

Exhibit A

21ella
Sequencher™ "21ellracefinal"



21ella
Sequencer™ "21ellracefinal"

R1 GQCTAGCCTG TCCTGACAGG GGAGAGTTAA GCTCCCGTTC TCCACCGTGC CCGCTGQCCA GGTGGGCTGA GGSTGACCA GAGACCAGAA
 G P V L T G E S . A P V L H R A G M P G Q L R V T E R P E

091 CCTGCTTGGT GAGGCTTAGT GTCTAGAGCT GGCGAAGGAG GTTCGCCGC TCCTCTGTG TACGCGCCG CAGCCGCTCC CGGCTTCACT
P A C W S L V L R A Q E G G S A A P L L S A P A A P P G P T
+ + + + + + + + + + + + + + +

#181. TCCTCCGCGCA GCCCCTGCTA CTGAGAAGCT CCGGGATCCC AGCAACGCC CCAGCCCTGC CTCAGCCTGC GGGGCTCCAG TCAAGCCAAC
S S N S P C Y . X A P G S Q Q P P R P Q L S L R G S S Q A N
.

[illegible]

0271. ACCGACGCCGCG AGCTGCGGAGG AAGACAGGAC CCTTGACATC TCCATCTGCA CAGAGGCTCT GCTCTGAGCCG AGCAGGCTCC TCCTCCTAGG
T D A Q L G G R Q D P . H L N L N R G P G W T R Q P P P P R
T T T T

[illegible]

21ella
Sequences "21ella" "21ella" "21ella"

21chsa103p2v2 >#1>

79

0361 ATGACCTCAC CCTCCAGCTC TCCAGTTTTC AGGTTGAGA CATTAGATGG AGGCCAAGAA GATGCTCTG AGGCGGACAG AGGAAAGCTG
M T S P S S S P V P R L E T L D G Q Q E D Q S E A D R G E L
.. .. .

[illegible]

21ella
Sequencher™ "21ell1racefinal"

```

jchsa103a2d1 >#1> TTTCGGA CCGGNCCTGCH TCCCATGAG TCACAGTTCC AGGNCGAGGA CCGGAAATTC GCCCTCAGA TAAGAGTCAC CCTCAACTAC
f1h21ell1r18 >#1> TGGC TCCCATGGAG TCACAGTTCC AGGCGAGGA CCGGAAATTC GCCCTCAGA TAAGAGTCAC CCTCAACTAC
f1h21ell1r21 >#1> AG TCACAGTTCC AGGNCGAGGA CCGGAAATTC GCCCTCAGA TAAGAGTCAC CCTCAACTAC
f1h21ell1r27 >#1> AG TCACAGTTCC AGGCGAGGA CCGGAAATTC GCCCTCAGA TAAGAGTCAC CCTCAACTAC
f1h21ell1r22 >#1> TCACAGTTCC AGGCGAGGH CCGGAAATTC GCCCTCAGA TAAGAGTCAC CCTCAACTAC
f1h21ell1r1 >#1> TCC A:GGCGAGGH CCGGAAATTC GCCCTCAGA TAAGAGTCAC CCTCAACTAC
GenBank AA4 >#1> AGGCGAGGA CCGGAAATTC CTCAGA TAAGAGTCAC CCTCAACTAC
f1h21ell1r1 >#1> AGGNCGAGGA CCGGAAATTC GCCCTCAGA TAAGAGTCAC CHTCAACTAC
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f1h21ell1r1 >#1> GGC:AGG: HCGGAAATTC GCCCTCAA TAAGAGTCAC CCTCAACTAC
GenBank AA4 >#1> GGA CCGGAAATTC CTCAGA TAAGAGTCAC CCTCAACTAC
GenBank AA2 >#1> TC GCCCTCAGA TAAGAGTCAC CCTCAACTAC
jchsa103a2w1 >#1> TAC

```

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P P Q S G L P P M B S Q P Q Q E P R E P A P Q I R V E L N Y
. . . . .

```

[illegible]

21ella
Sequencer™ "21ellracefinal"

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|--------------------|-------------|------------|-----------|------------|------------|------------|-------------|-------------|------------|
| FlhKZ1el1T74- #49 | CGAAAGGGAA | CAGGTGCCA | TCAACCGAT | CCAAACCGAT | TTGACCGAGA | TGCGCTCTTC | AAATCGGCTCT | CCCGGGGTGT | CCCCGAGAT |
| Gembank AA81- 14 | CGAAAGGGAA | CAGGTGCCA | TCAACCGAT | CCAAACCGAT | TTGACCGAGA | TGCGCTCTTC | AAATCGGCTCT | CCCGGGGTGT | CCCCGAGAT |
| Gembank AA23- #35 | CGAAAGG; AA | CAGGTGCCAG | TCAACCGAT | CCAAACCGAT | TTGACCGAGA | TGCGCTCTTC | AAATCGGCTCT | CCCGGGGTGT | CCCCGAGAT |
| JChn103e2w1 04 | HGAAAGGGAA | CAGCTGCCAG | TCAACCGAT | CCAAACCGAT | TTGACCGAGA | TGCGCTCTTC | AAATCGGCTCT | CCCGGGGTGT | CCCCGAGAT |
| FlhKZ1el1T79- #41> | AAAGGGAA | CAGGTGCCAG | TCAACCGAT | CCAAACCGAT | TTGACCGAGA | TGCGCTCTTC | AAATCGGCTCT | CCCGGGGTGT | CCCCGAGAT |
| JChn103e2w2 #41> | | | CAG | TCAACCGAT | CCAAACCGAT | TTGACCGAGA | TGCGCTCTTC | AAATCGGCTCT | CCCGGGGTGT |
| Gembank AY0- #41> | | | | | | | CT | CCCGGGGTGT | CCCCGAGAT |

[illegible]

21e11a

Sequencer™ "21611racefinal"

[illegible]

721 ATGAAGCGCTG TGCTGAACCT CAAAGGACGGA GTCAATGCGT GCATTCTGCG ACTGCTGCAG ATCGACAGGG ACTCTGGGAA TCCTCAGCCC
N K A V L N L E D G V N A C I L P L L Q I D R P S G N P Q P

21ella
Sequencher™ "21ellracefinal"

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2 Genbank AA7 0392 CTGGTAAATG CCCAGTGCAC AGATGACTAT TACCGAGGCC ACAGCGCTCT GCACATCGCC ATT
3 Genbank AA7 0369 CTGGTAAATG CCCAGTGCAC AGATGACTAT TACCGAGGCC ACAGCGCTCT GCACATCGCC ATT
4 Flnh21e11r12 0368 CTGGTAAATG CCCAGTGCAC AGATGACTAT TACCGAGGCC ACAGCGCTCT GCACATCGCC ATTGAGAAAG GAGTCTGCA GTGTGTGAAQ
5 Flnh21e11r19 0368 CTGGTAAATG CCCAGTGCAC AGATGACTAT TACCGAGGCC ACAGCGCTCT GCACATCGCC ATTGAGAAAG GAGTCTGCA GTGTGTGAAQ
6 Genbank A11 0366 CTGGTAAATG CCCAGTGCAC AGATGACTAT TACCGAGGCC ACAGCGCTCT GCACATCGCC ATTGAGAAAG GAGTCTGCA GTGTGTGAAQ
7 jchsa103e02u 0363 CTGGTAAATG CCCAGTGCAC AGATGACTAT TACCGAGGCC ACAGCGCTCT GCACATCGCC ATTGAGAAAG GAGTCTGCA GTGTGTGAAQ
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15 Genbank AA2 0303 CTGGTAAATG CCCAGTGCAC AGATGACTAT TACCGAGGCC ACAGCGCTCT GCACATCGCC ATTGAGAAAG GAGTCTGCA GTGTGTGAAQ
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L V N A Q C T P D Y Y R Q B S A L H I A I E K R S L Q C V K

(901) CTCTGTGTGG AGAATGGGGC CAATGTGCAT GCCCCGGGCTT GCGGGCGCTT CTTCAGAGG GCGCAAGGGA CTTCCTTTTA TTTCGGTGAG
L L V E N G A M V N A R A C G R F Y Q K G Q G T C F Y F G E

#1081 ACTGACTCCC AGGGCAACAC AGTCCTGCAT GCCCTAGTGA TGATCTCGGA CAACTCAQCT GAGAACATTG CACTGGTGAC CAGCATGTAT
T D S Q G N T V L H A L V M I S D N S A E N I A L V T S M Y
T T T T T

21ella
Sequences "21ellracfinal"

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Gembank W38... >117

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1231 GCGGCCAAGG AGGGCAAGAT CGAGATTTTC AGGCACATCC TGCAAGCGGA GTTTTCAGGA CTGAGCCACC TTTCGCCAAA GTTCACCGAG
Gembank AA3... 1279 GCGGCCAAGG AGGGCAAGAT CGAGATTTTC AGGCACATCC TGCAAGCGGA GTTTTCAGGA CTGAGCCACC TTTCGCCAAA GTTCACCGAG
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Gembank AA3... >117

11261 GCGGCCAAGG AGGGCAAGAT CGAGATTTTC AGGCACATCC TGCAAGCGGA GTTTTCAGGA CTGAGCCACC TTTCGCCAAA GTTCACCGAG
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Gembank AA35... 1438 TGGTGCTATG GGGCTGTCCG GGTGTGCTCG TATGACCTGG CTCTGTGGA CAGCTGTGAG GAGAACTCAG TGCTGAGAT CATTCGCTTT
1417 GGGCTGTGCG GGTGTGCTCG TATGACCTGG CTCTGTGGA CAGCTGTGAG GAGAACTCAG TGCTGAGAT CATTCGCTTT
Gembank W38... 1417

11351 TGGTGCTATG GGGCTGTCCG GGTGTGCTCG TATGACCTGG CTCTGTGGA CAGCTGTGAG GAGAACTCAG TGCTGAGAT CATTCGCTTT
W C Y G F V R V S L Y D L A S V D S C R E H S V L E I I A F

1501 CATTGCAAGA GCGCCGACCG ACACCGAATG GTCGTTTTGG AGCCCTGAA CAAACTGCTG C
1501 CATTGCAAGA GCGCCGACCG ACACCGAATG GTCGTTTTGG AGCCCTGAA CAAACTGCTG CAGGCGAAAT GGGATCTGCT CATCCCCAAG
1493 CATTGCAAGA GCGCCGACCG ACACCGAATG GTCGTTTTGG AGCCCTGAA CAAACTGCTG CAGGCGAAAT GGGATCTGCT CATCCCCAAG
1497 CATTGCAAGA GCGCCGACCG ACACCGAATG GTCGTTTTGG AGCCCTGAA CAAACTGCTG CAGGCGAAAT GGGATCTGCT CATCCCCAAG
Gembank W38... 1245 CATTGCAAGA GCGCCGACCG ACACCGAATG GTCGTTTTGG AGCCCTGAA CAAACTGCTG CAGGCGAAAT GGGATCTGCT CATCCCCAAG
Gembank AA3... 1128 CATTGCAAGA GCGCCGACCG ACACCGAATG GTCGTTTTGG AGCCCTGAA CAAACTGCTG CAGGCGAAAT GGGATCTGCT CATCCCCAAG
1491 CATTGCAAGA GCGCCGACCG ACACCGAATG GTCGTTTTGG AGCCCTGAA CAAACTGCTG CAGGCGAAAT GGGATCTGCT CATCCCCAAG
Gembank W38... 131 CATTGCAAGA GCGCCGACCG ACACCGAATG GTCGTTTTGG AGCCCTGAA CAAACTGCTG CAGGCGAAAT GGGATCTGCT CATCCCCAAG

11441 CATTGCAAGA GCGCCGACCG ACACCGAATG GTCGTTTTGG AGCCCTGAA CAAACTGCTG CAGGCGAAAT GGGATCTGCT CATCCCCAAG
H C K S P H R H R H V V L E P L H K L L Q A K W D L L I P E

21ella
Sequencher™ "21ellracefinal"

Adm21ell - #425 GGCCTAAGC CAGATGGCAG CCCGGATGAG CCTGCTGCT TCAGGGTGA GAGGTGAAC TGGGCTTCAT GGGAGCAGAC GCTGCTACG
frmb12c4d1... #41> TCAT GGGAGCAGAC GCTGCTACG

#2431 GGCCTAAGC CAGATGGCAG CCCGGATGAG CCTGCTGCT TCAGGGTGA GAGGTGAAC TGGGCTTCAT GGGAGCAGAC GCTGCTACG
G T K P D G S P D S R W C P X V E E V N W A S W S Q T L P T

Adm21ell - #515 CTCGTGTAGG ACCCGTCAGG GGCAGGTCTC CCTCGAATC TCAGAGACCC TGTCTGCT TCCCTCCCA AGGAGGATGA GATGCTGCC
frmb12c4d1... #25 CTCGTGTAGG ACCCGTCAGG GGCAGGTCTC CCTCGAATC TCAGAGACCC TGTCTGCT TCCCTCCCA AGGAGGATGA GATGCTGCC

#2531 CTCGTGTAGG ACCCGTCAGG GGCAGGTCTC CCTCGAATC TCAGAGACCC TGTCTGCT TCCCTCCCA AGGAGGATGA GATGCTGCC
L C E D P S G A G V P R T L E N P V L A S P P E E D E D G A

Adm21ell - #605 TCTGAGGAAA ACTATGTGCC CGTCAGCTC CTCAGTCCA ACTGATGGC CAGATGCAGC AGGAGGCCAG AGGACAGAGC AGAGGATCTT
frmb12c4d1... #115 TCTGAGGAAA ACTATGTGCC CGTCAGCTC CTCAGTCCA ACTGATGGC CAGATGCAGC AGGAGGCCAG AGGACAGAGC AGAGGATCTT

#2611 TCTGAGGAAA ACTATGTGCC CGTCAGCTC CTCAGTCCA ACTGATGGC CAGATGCAGC AGGAGGCCAG AGGACAGAGC AGAGGATCTT
S E E N Y V P V Q L L Q S N W P H C S R R P E D R A E D L

Adm21ell - #695 TCCAACCACA TCTGCTGCT CTGGGCTCCC AGTGAATTCT GGTGGCAAAT ATATATTTTC ACTAACTCAA AAAAAAAAAA AAAAA
frmb12c4d1... #205 TCCAACCACA TCTGCTGCT CTGGGCTCCC AGTGAATTCT GGTGGCAAAT ATATATTTTC ACTAACTCAA AAAAAAAAAA AAAAAAAAAA

#2701 TCCAACCACA TCTGCTGCT CTGGGCTCCC AGTGAATTCT GGTGGCAAAT ATATATTTTC ACTAACTCAA AAAAAAAAAA AAAAAAAAAA
S N H I C W L W G F S E P W W Q I Y I P T N S K K K K K K K

frmb12c4d1... #295 AAAAAAAAAA AAAAAAAAAA

#2791 AAAAAAAAAA AAAAAAAAAA
K K K K K K

Exhibit C

BLASTP vs. PNU (AA) flh2lellorfaa - 5:26:57 pm on Dec 21 98

BLASTP 1 4.10MP-WashU [30-Aug-96] [Build 20:24:58 Oct 21 1996]

Reference: Altschul, Stephen F., Warren Gish, Webb Miller, Eugene W. Myers, and David J. Lipman (1990). Basic local alignment search tool. J. Mol. Biol. 215:403-10.

Query= flh2lellorfaa
(764 letters)

Database: /disk0/asap/databases/db/NRP/protxnu
345,099 sequences; 106,000,184 total letters.
Searching.....done

| Sequences producing High-scoring Segment Pairs: | High
Score | Smallest
Sum
Probability
P(N) | N |
|---|---------------|--|---|
| GP:gi 2570933 (AF029310) vanilloid receptor subtype 1 [Ra... | 336 | 1.9e-221 | 7 |
| GPU:gi 3986159 gnl PID d1035925 (AB015231) VR1sk [Mus mus... | 299 | 9.8e-136 | 6 |
| GP:gi 2911863 (AF047660) contains similarity to ankyrin r... | 103 | 6.5e-20 | 8 |
| GP:gi 3675319 gnl PID e1344970 (Z74030) similar to ankyri... | 97 | 1.1e-19 | 7 |
| GP:gi 2642590 (AF031408) olfactory channel [Caenorhabditi... | 93 | 3.6e-16 | 6 |
| GP:gi 2854148 (AF045639) contains similarity to ankyrin r... | 93 | 4.1e-16 | 6 |
| GP:gi 3879753 gnl PID e1349345 (Z72514) Similarity to Hum... | 73 | 3.6e-11 | 6 |
| GP:gi 3267188 gnl PID e315126 (Y10601) ankyrin-like prote... | 71 | 2.7e-08 | 6 |
| SP:SP:sp P48994 TRPL_DROME TRANSIENT-RECEPTOR-FCNTENTIAL L... | 69 | 2.2e-05 | 4 |
| GP:gi 1841966 (U65916) ankyrin [Rattus norvegicus] | 72 | 5.6e-05 | 3 |

WARNING: Descriptions of 4 database sequences were not reported due to the limiting value of parameter V = 11.

>GP:gi|2570933 (AF029310) vanilloid receptor subtype 1 [Rattus norvegicus]
Length = 838

Score = 336 (156.0 bits), Expect = 1.9e-221, Sum P(7) = 1.9e-221
Identities = 67/112 (59%), Positives = 84/112 (75%)

Query: 206 FYFGELPLSLAACTKQWDVVSYLENEHQPASLQATDSQGNVTLHALVMISDNSEAENIAL 265
FYFGELPLSLAACT C +V +LL+N QPA + A DS GNTVLHALV ++DN+ +N
Sbjct: 245 FYFGELPLSLAACTNQLAIVKELLQNSWQPADISARUSVENTVLHALVEVADNTVDINTKF 304

Query: 266 VTSMYDQLLQAGARLCPTVQLEDIRNLQDLTFLKLAKEGKIBIFRHILORE 317
VTSMY+ +L GA+L PT++LE+I N + LTPL LAA GKI + +ILORE
Sbjct: 305 VTSMYNEILILGAKLHPTLKLREITNRKGLTPLALAASSGKIGVLAYILORE 356

Score = 316 (146.7 bits), Expect = 1.9e-221, Sum P(7) = 1.9e-221
Identities = 65/138 (47%), Positives = 93/138 (67%)

Query: 66 ASQPDPNRFRDRFLFNAVSRGVPEDLAGLFEYLSKTSKYLTDSEYTEGSTGKTCMLKAVL 125
A + P +DR +F+AV++ ++L L +L ++ K LTDSE+ + TGKTCCL+KA+L
Sbjct: 104 AGEKPFRLYDRRSIFDAVAQSNQCELESLL+FLQSKKRLTDSEFKDPETGKTCCLKAML 163

Query: 126 NLKDGVNACILPLLQIDRDSGNFQPLVNAQCTDDYYRGHSALHIAIEKRSIQCVKLLVEN 185
NL +G N I LL + R + + + VNA TD YY+G +ALHIAIE+R++ V LLVEN
Sbjct: 164 NLHNCQNDTIALLLDVARKTDSLKQFVNAS+TDSYYKGQTALHIAIEFRNMTELVTLLEN 223

Query: 186 GANVHARACGRFPQKQGQ 203

GA+V A A G FF+K +G

Sbjct: 224 GADVQAAANGDFFKKTG 241

Score = 299 (138.8 bits), Expect = 1.9e-221, Sum P(7) = 1.9e-221
 Identities = 69/175 (39%), Positives = 94/175 (53%)

Query: 391 FFLNELCNLIYMFISTAVAYHOPTLKKAAAPHLKAEVGNMMLLTGHILILLGGIYLLVGQL 450
 F+ NF +YM IFTA AY++P LK VG+ +TG IL + +

Sbjct: 434 FYFNFPVYCLYMIIFTAAAYYRPFVEGLEFPYKLNKTVGDYFRVTGEILSVXXXXXXXKGI 493

Query: 451 WYFWRHVFIIWISFIDSVEILFLFQALLKPVSVLCLFLATEWYLPILLVSALVLGWLNL 510
 YF +R + F+DSY EILF Q+L VS VL F + Y+ +V +L +GW N+L

Sbjct: 494 QYFLQRRPSLKSLEFVDSYSEILFPVQSLF.LVSVLYFSQRKEYVASMVFLAMGWITNL 553

Query: 511 YYTRGFQHTGIYSVMIOKVILRDLRPLLIYLVFLPGPAVALVSLSQEAWRPEAP 565
 YYTRGFQ GIY+VMI+K+ILRDL R A+V+L ++ P

Sbjct: 554 YYTRGFQQMGIVAVMIKMIILRDLRXXXXXXXKXTAVVTLIEDGKNNSLP 602

Score = 281 (130.5 bits), Expect = 1.9e-221, Sum P(7) = 1.9e-221
 Identities = 54/95 (56%), Positives = 70/95 (73%)

Query: 586 GAQYRGILEASLELFKFTIGMGELAFQEQHFRGMVLLILLAYVLLTYILLNMLIALME 645
 G Y + LELFKFTIGMG+L F E F+ + +LLAYV+LTYILLNMLIALM

Sbjct: 624 GNSYNSLYSTCLELFKFTIGMGDLFTENYDFKAVFIILLAYVILTYILLNMLIALMG 683

Query: 646 ETVNSVATDSWSIWKLOKAIISVLEMENGYWWCRKK 680
 ETVN +A +S +IWKLO+AI++L+ E + C +K

Sbjct: 684 ETVNKIAQESKNIWKLOKRAITILDTEKSFLLKMRK 718

Score = 162 (75.2 bits), Expect = 1.9e-221, Sum P(7) = 1.9e-221
 Identities = 28/38 (73%), Positives = 34/38 (89%)

Query: 323 HLSRKFTWCYGFVRVSLYDLASVDSCEZNSVLEIIAP 360
 HLSRKFTFW YGPV SLYDL+ +D+CE+NSVLE+IA+

Sbjct: 364 HLSRKFTWAYGPFVHSSLYDLSCIDTCEKNSVLEVIAY 401

Score = 144 (66.9 bits), Expect = 1.9e-221, Sum P(7) = 1.9e-221
 Identities = 25/47 (53%), Positives = 31/47 (65%)

Query: 678 RKKQRAGVMLTVGTXPDGSPDERWCPRVEEVNWASWEOTLPTLCEDF 724
 RK R+G +L VG PDG D RWCPRV+EVNW +W + + EDP

Sbjct: 717 RKAFRSGKLLQVGSTPDGKDDYRWCFRVEVNWTWNTNVGIINEDF 763

Score = 94 (43.6 bits), Expect = 1.9e-221, Sum P(7) = 1.9e-221
 Identities = 15/30 (50%), Positives = 24/30 (80%)

Query: 363 KSPHRHRMVVLEPLNKLQAKWDLIPKFF 392
 ++P+RH M+++EPLN+LLQ KWD + + F

Sbjct: 405 ETPNRHDMILLVEPLNRLQDKWDRFVKRIF 434

Score = 46 (21.4 bits), Expect = 1.3e-162, Sum P(6) = 1.3e-162
 Identities = 11/48 (22%), Positives = 24/48 (50%)

Query: 435 HILILLGGIYLLVGQLWYFWRHVFIIWISFIDSVEILFLFQALLKPV 482
 H ++L+ + L+ W + + +F + F+ + I+F A +FV

Sbjct: 410 HDMILLVEPLNRLQDKWDRFVKRIFYFNFFVYCLYMIIFTAAAYYRPV 457

Score = 37 (17.2 bits), Expect = 2.4e-169, Sum P(7) = 2.4e-169
 Identities = 8/22 (36%), Positives = 13/22 (59%)

Query: 297 PLKLAKEGKI2IPRHILQREF 318
 PL LAA ++ I + +IQ +

Sbjct: 251 PLSLAACINQLAIVKFLQNSW 272

Score = 37 (17.2 bits), Expect = 1.9e-111, Sum P(7) = 1.9e-111
Id ntities = 8/26 (30%), Positives = 15/26 (57%)

Query: 206 FYFGELPLSLAACTKQWDVVSYLEN 231
+Y G+ L +A + +V+ L+EN
Sbjct: 198 YXGQTALHIAIERRNMTLVTLIVEN 223

>GPU:gi|3986159|gnl|PID|d1035925 (AB015231) VR1sk [Mus musculus]
Length = 563

Score = 299 (138.8 bits), Expect = 9.8e-136, Sum P(6) = 9.8e-136
Identities = 69/175 (39%), Positives = 94/175 (53%)

Query: 391 FFLNFLCNLIYMFIFTAVAYHQPTLKKAAPHKAEVGNMILLTCHILILLGGIYLLVGQL 450
F+ NF +YM IPTA AY++P LK VG+ +TG IL + +
Sbjct: 127 FYFNFFVYCLYMIIFTAAAYRFEVGLPPYKLNITVGDYPRVTGEILSVXXXXXXXXXRG 186

Query: 451 WYPWRRHVPIWISFIDSYPFIFLFLQALLKPVSOVLCLALIEWVLPLVLSALVLGWLNL 510
YF +R + P+DSV RILF Q+L VS VL F + Y+ +V +L +GW N+L
Sbjct: 187 QYFLQRRPSLKSFLVDSYSEILFFVQSLFMLVSVVLYFSQRKEVVASNVFSLANGWINML 246

Query: 511 YYTRGFQHTGIYSVMIOKVILRDLLRELLIYLVFLFGFAVALVSLSQZAWRPEAP 565
YYTRGSQ GIY+VMI+K+ILRD L A+V+L ++ P
Sbjct: 247 YYTRGFQOMGIYAVMIRKMLILRDLCRXXXXXXXXXXXXTAVVTLIEDGKNNSLP 301

Score = 253 (117.5 bits), Expect = 9.8e-136, Sum P(6) = 9.8e-136
Identities = 50/89 (56%), Positives = 64/89 (71%)

Query: 586 GAQYRGILEASLELFKFTIGMGELAFQEQHFRGMVLLLLLAYVLLTYILLINMLIALMS 645
G Y + LELEKFTIGMG+L P E F+ + +LLAYV+LTYILLINMLIALM
Sbjct: 317 GNSYNSLYSTCLELFKFTIGMGDLFTENYDFKAVFIILLAYVILTYILLINMLIALMG 376

Query: 646 ETVNSVATDSWSIWKLQKALSULEMENGY 674
ETV V+ +S IWKLQ A ++L++E +
Sbjct: 377 ETVGQVSKESKHIWKLQWATTILDIERSF 405

Score = 163 (75.7 bits), Expect = 9.8e-136, Sum P(6) = 9.8e-136
Identities = 28/47 (59%), Positives = 34/47 (72%)

Query: 678 RKKQRAGVMLTVGTPDGSPDERWCPRVEEVNWSWEQTLPTLCEDP 724
RK R+G M+TVG DG+PD RWCPRV+EVNW+ W Q L + EDP
Sbjct: 410 RKAFRSGEMVTGKSSDGTDPDRRWCFRVEEVNWSHWNQNLGIINEDP 456

Score = 162 (75.2 bits), Expect = 9.8e-136, Sum P(6) = 9.8e-136
Identities = 28/38 (73%), Positives = 34/33 (89%)

Query: 323 HLSRKFTWCYGPVRVSLYQLASVDSCEENSVEIITAF 360
HLSRKFTW YGFP SLYDL+ +D+CE+NSVLE+IA+
Sbjct: 57 HLSRKFTWYGPVHSSLYDLSCIDTCEKNSVLEVIAY 94

Score = 129 (59.9 bits), Expect = 9.8e-136, Sum P(6) = 9.8e-136
Identities = 27/49 (55%), Positives = 36/49 (73%)

Query: 269 MYDGLLQAGARLCPTVQLEDIRNLQDLTPLKLAKEGKIEIFRHILORE 317
MY+ +L GA+L PT++LE+I N + LTPL IAA GKI + +ILORE
Sbjct: 1 MYNEIILGAKLHPTLKLREETNRKGLTPLALAASSGKIGVLAYILORE 49

Score = 94 (43.6 bits), Expect = 9.8e-136, Sum P(6) = 9.8e-136
Identities = 15/30 (50%), Positives = 24/30 (80%)

Query: 363 KSPHRHRMVVLEPLNKLLOAKNDLLIPKFP 392

Query: 98 ETPNRHDMLLVEPLNRLLOQCKWDRFVKRI 127
 Sbjct: 98 ETPNRHDMLLVEPLNRLLOQCKWDRFVKRI 127

Score = 46 (21.4 bits), Expect = 2.3e-77, Sum P(5) = 2.3e-77
 Identities = 11/46 (22%), Positives = 24/46 (50%)

Query: 435 HILILGCTYLLVQQLWYFWRHVFIIWISFIDSYPFELFLQALLKPV 482
 H ++L+ + L+ W + + +P + E+ + I+E A +PV
 Sbjct: 103 HDMLLVEPLNRLLOQCKWDRFVKRIFYFNFFVYCLYMIIFTAAAYYRPV 150

Score = 42 (19.5 bits), Expect = 1.2e-122, Sum P(6) = 1.2e-122
 Identities = 9/22 (40%), Positives = 16/22 (72%)

Query: 209 GELPLSLAACTKQWDVVSYLLE 230
 G PL+LAA + + V++Y+L+
 Sbjct: 26 GLTPLALAASSGKIGVLAYILQ 47

>GF:gi|2911863 (AF047660) contains similarity to ankyrin repeats
 [Caenorhabditis elegans]
 Length = 900

Score = 103 (47.8 bits), Expect = 6.5e-20, Sum P(8) = 6.5e-20
 Identities = 23/29 (25%), Positives = 44/29 (49%)

Query: 497 LLVSALVLGWLNLIIYYTRGFQHTGIYSVMIOKVILRDLLRFLIIYLVFLGFAVALVSL 556
 L+ ++ ++ LYY R + G + +M+ +I D+ RF+LTY +PL GF+ + +
 Sbjct: 592 LITVTMIPTTVHYLYYCRVIRFVGPFVLMVYTIATDIFRPMIYGIPLMGFSQSFSLIF 651

Query: 557 QEAWRPEAPTGPNTESVQPMEGQEDEGN 585
 R + + EG +++ N
 Sbjct: 652 LSCEREANVIKKLITDOSEASEGSDNKEN 680

Score = 63 (29.3 bits), Expect = 6.5e-20, Sum P(8) = 6.5e-20
 Identities = 15/27 (55%), Positives = 18/27 (66%)

Query: 291 NLQDLTFLKLAKEGRIEIRHILQRE 317
 N Q L+PL LAAK K E+F IL+ E
 Sbjct: 328 NKQSLSPILTIAAKLAKKEMFDEILELE 354

Score = 56 (26.0 bits), Expect = 6.5e-20, Sum P(8) = 6.5e-20
 Identities = 16/48 (33%), Positives = 25/48 (52%)

Query: 151 LVNAOCTODVYRHSALHIAIEKRSLOQVALLVENGANVHARACGRFP 158
 L+N + + G S LH AI + V ++ GA+V++R G FF
 Sbjct: 185 LLNDIHTISZDFYGLSPLHQAIIPTDCKLVYKFLKLGADVNSRCYGAF 232

Score = 54 (25.1 bits), Expect = 6.5e-20, Sum P(8) = 6.5e-20
 Identities = 12/23 (52%), Positives = 13/23 (56%)

Query: 207 YFGELPLSLAACTKQWDVVSYLL 229
 Y GE PLS AAC Q + LL
 Sbjct: 263 YLGEYPLSFAACLNQPEPRLL 285

Score = 49 (22.8 bits), Expect = 6.5e-20, Sum P(8) = 6.5e-20
 Identities = 8/23 (34%), Positives = 12/23 (52%)

Query: 331 WCYGPVRVSLYDLASVDSCEPNS 353
 W YG + Y LA +D+ E +
 Sbjct: 359 WAYGDASSTAYPLAKIDTINETT 381

Score = 47 (21.8 bits), Expect = 6.5e-20, Sum P(8) = 6.5e-20
 Identities = 11/30 (36%), Positives = 18/30 (60%)

Query: 236 ASLOATDSQGNVTLHALVMISDENSENIAL 265
 A+ A D+ GN+VLH V+ + + +AL
 Sbjct: 289 ANFNAQDTNGNSVLHMCVIHENMAMFKLAL 318

Score = 46 (21.4 bits), Expect = $5.7e-15$, Sum P(6) = $5.7e-13$
 Identities = 9/27 (33%), Positives = 17/27 (62%)

Query: 163 GHSALHIAIEKRSLOQCVKLLVENGANV 189
 G+S LH+ + ++ KL +E GA++
 Sbjct: 298 GNSVLHMCVIHENMAMFKLALCCGASL 324

Score = 43 (20.0 bits), Expect = $6.5e-20$, Sum P(8) = $6.5e-20$
 Identities = 8/18 (44%), Positives = 13/18 (72%)

Query: 634 ILLNMLIALMSETVNSV 651
 I+ NMLIA+M+ T ++
 Sbjct: 753 IMQFNMLIAMTETTYETI 770

Score = 41 (19.0 bits), Expect = $6.5e-20$, Sum P(8) = $6.5e-20$
 Identities = 10/27 (37%), Positives = 16/27 (59%)

Query: 113 GSTGKTCLMKAVLNKDGVNACILPLL 139
 GS G+T + +L+ D NA +L +L
 Sbjct: 153 GSMGETIIGCCILHASDIENALVLKIL 179

Score = 35 (16.3 bits), Expect = 0.00016, Sum P(3) = 0.00016
 Identities = 9/37 (24%), Positives = 16/37 (43%)

Query: 67 SQPDPNRFRDRRLFNAVSRGVPEDLAGLPEVLSKTSK 103
 S+P P R+ ++ V + GL E+ S+
 Sbjct: 464 SEFFFRGRYGNSTLQOVKPVINATSRGLVEWSEPLSQ 500

Score = 34 (15.8 bits), Expect = $6.8e-11$, Sum P(8) = $6.8e-11$
 Identities = 8/31 (25%), Positives = 17/31 (54%)

Query: 422 LKAEVENSMLLTGHILILGGIYLLVGQLWY 452
 L ++ +L+ ++LI + I+ V L+Y
 Sbjct: 577 LACDLSPVLLVVDNVLITVTMIPTTVHYLY 607

>GP:gi|3675319|gnl|PID|e1344970 (274030) similar to ankyrin repeats
 [Caenorhabditis elegans] >GP:gi|3876480|gnl|PID|e1346172 (272508)
 similar to ankyrin repeats [Caenorhabditis elegans]
 Length = 790

Score = 97 (45.0 bits), Expect = $1.1e-19$, Sum P(7) = $1.1e-19$
 Identities = 18/53 (33%), Positives = 32/53 (60%)

Query: 497 LLVSALVLGWLNLIIYYTRGFQKGTGIYSVMIQKVIIRDLLRFLIIYLVFLFGFA 549
 + + +++L + LYY R G + +M+ +I DL+RF +IY +FL GF+
 Sbjct: 526 MAIISILLVTQHFLYYMRAIPFVGPFVLMVYTIATDLVRFAMIVSIFLVGFS 578

Score = 89 (41.3 bits), Expect = $1.1e-19$, Sum P(7) = $1.1e-19$
 Identities = 19/48 (39%), Positives = 27/48 (56%)

Query: 151 LVNAQCTDDYYRGHSALHIAIEKRSLOQCVKLLVENGANVHARACGRFF 198
 L+N C + Y G S LH+AI + Q LL+ GA+++ R G FF
 Sbjct: 189 LINDICVSEYVYGLSPLHLAIVNQDAQFTSILLRLGADLNQRCYGAFF 236

Score = 62 (28.8 bits), Expect = $1.1e-19$, Sum P(7) = $1.1e-19$
 Identities = 13/23 (56%), Positives = 14/23 (60%)

Query: 207 YFGELPLSLAACTKQWDVVSyll 229
YFGE PLS A C Q D+ LL
Sbjct: 267 YFGEYPLSPAICMGQHDLFRLML 289

Score = 51 (23.7 bits), Expect = 1.1e-19, Sum P(7) = 1.1e-19
Identities = 10/19 (52%), Positives = 13/19 (68%)

Query: 236 ASLQATDSQGNLVLHALVM 254
A+L A D+ GNT LH V+
Sbjct: 293 ANLSAQDTMGNTALHLCVI 311

Score = 49 (22.6 bits), Expect = 1.1e-19, Sum P(7) = 1.1e-19
Identities = 11/51 (21%), Positives = 27/51 (52%)

Query: 601 KPTIGNGELAFQEQHFRGMVLLLLAYVLLTYILLNMLIALMSPTVNSV 651
+E++ E++ + + + L+ + + IL N+LIA+M+ T ++
Sbjct: 626 EFSVLRYREMSACDNFWMKWLKIFVIFETP/SILOFNLLIAMMTRTYETI 676

Score = 43 (20.0 bits), Expect = 1.2e-06, Sum P(5) = 1.2e-06
Identities = 7/27 (25%), Positives = 16/27 (59%)

Query: 163 GHSALHIAIEKRSLQCVKLLVENGANV 189
G++ALH+ + + +E G N+
Sbjct: 302 GNTALHLCVINDKMDMLDAVLEAGNT 328

Score = 39 (18.1 bits), Expect = 5.5e-12, Sum P(7) = 5.5e-12
Identities = 12/56 (21%), Positives = 25/56 (44%)

Query: 461 WISFIDSYPEILFLFQALLKPVSVQLCFIAIEWYLLVLSALVLGWLNLLYYTRGF 516
W +E+ ++ L A L + + C LA ++ L + +++L T+ F
Sbjct: 483 WFNPLKAPPAKLMFKGASLFIIISIPCLACSFHEFFLTIDNTMAIISILLVTOHF 538

Score = 38 (17.6 bits), Expect = 1.1e-19, Sum P(7) = 1.1e-19
Identities = 9/18 (50%), Positives = 12/18 (66%)

Query: 289 IRLQDITPLKLAARKPK 306
+ N Q+LT L LAA+ K
Sbjct: 330 LANKQNLTAITLAARLAK 347

Score = 37 (17.2 bits), Expect = 4.7e-18, Sum P(7) = 4.7e-18
Identities = 7/15 (46%), Positives = 9/15 (60%)

Query: 723 DPGAGVPRITLENPV 737
DP G+ +ENPV
Sbjct: 599 DPMGSEFNNTMENPV 613

Score = 36 (16.7 bits), Expect = 1.1e-19, Sum P(7) = 1.1e-19
Identities = 10/47 (21%), Positives = 16/47 (34%)

Query: 376 LNKLLQAKWDLIPKFFLNFLCNLIYMFISTAVAYHQPTLKKAAPHL 422
+ ++L KW +L L I+ + AY HL
Sbjct: 362 IEQILDEKWKAYGRALWLSLLGFIFPYCCFVCAYMLRPSSATTEHL 408

Score = 35 (16.3 bits), Expect = 3.0e-08, Sum P(6) = 3.0e-08
Identities = 9/23 (39%), Positives = 11/23 (47%)

Query: 207 YFGELPLSLAACTKQWDVVSyll 229
Y+G PL LA + S LL
Sbjct: 199 YYGLSPLHLAIVNQDAQFTSLLL 221

Score = 34 (15.8 bits), Expect = 3.9e-12, Sum P(5) = 3.9e-12
Identities = 7/21 (33%), Positives = 13/21 (61%)

Query: 297 PLKLAKEGKIEIFRHILQRE 317
 PL A G+ ++FR +L ++
 Sbjct: 272 PLSFAICMGQHDLFRMLLAKK 292

Score = 34 (15.8 bits), Expect = $8.9e-10$, Sum P(7) = $8.9e-10$
 Identities = 6/18 (33%), Positives = 12/18 (66%)

Query: 610 AFQEQLHFRGMVLLLLLA 627
 AF +L F+G L +++++
 Sbjct: 489 APPAKLMFKGAPLFIIIS 506

Score = 34 (15.8 bits), Expect = $4.0e-08$, Sum P(6) = $4.0e-08$
 Identities = 11/40 (27%), Positives = 16/40 (40%)

Query: 153 NAOCTDDYYRGHSALHIAIEKRSLOQCVKLLVENGANVHAR 192
 N T Y G L AI ++L+ AN+ A+
 Sbjct: 259 NTNYTGSMYFGEYPLSFAICMGQHDLFRMLLAKKANLSAQ 298

>GP:gi|2642590 (AF031408) olfactory channel (Caenorhabditis elegans)
 Length = 937

Score = 93 (43.2 bits), Expect = $6.8e-16$, Sum P(5) = $6.8e-16$
 Identities = 19/36 (52%), Positives = 25/36 (69%)

Query: 163 GHSALHIAIEKRSLOQCVKLLVENGANVHARACGRFF 198
 G SALH+AI + V LL+ + A+V+ARACG FF
 Sbjct: 172 GQSALHLAIVHDDYETVSLLLNSKADVNARACGNFF 207

Score = 92 (42.7 bits), Expect = $6.8e-16$, Sum P(5) = $6.8e-16$
 Identities = 20/53 (37%), Positives = 31/53 (58%)

Query: 497 LLVSALVLGWLNLLYYTRGFQHTGIYSVMICKVILRDLLRFLLIYLVFLPGFA 549
 L V AL W+ LL++ R + TG + MI +I D++RF +I +FL F+
 Sbjct: 500 LFVVALPGSWIFLLFFARSAKLTGFFVQMTYSMIAGDMIRFAIISAIFLVSFS 552

Score = 57 (26.5 bits), Expect = $6.8e-16$, Sum P(5) = $6.8e-16$
 Identities = 10/24 (41%), Positives = 15/24 (62%)

Query: 207 YFGELPLSLAACTKQWDVVSYLLE 230
 Y+GE FL+ AAC D+ L++
 Sbjct: 226 YYGEYPLAFAACFGNKDIYDLLIQ 249

Score = 50 (23.2 bits), Expect = $6.8e-16$, Sum P(5) = $6.8e-16$
 Identities = 11/25 (44%), Positives = 15/25 (60%)

Query: 291 NLQDLTPLKLAKEGKIEIFRHILQ 315
 N TPL LA K G+ +IF +L+
 Sbjct: 294 NHAGFTPLTLATKLGRKQIFEEMLE 318

Score = 44 (20.4 bits), Expect = $6.8e-16$, Sum P(5) = $6.8e-16$
 Identities = 10/24 (41%), Positives = 15/24 (62%)

Query: 242 DSQGNVTIHALVMISDNDAENIAL 265
 DS GNT+LH V+ +S + A+
 Sbjct: 258 DSPGNTILHMCVINYSSSMYSYAV 281

Score = 37 (17.2 bits), Expect = $2.2e-05$, Sum P(4) = $2.2e-05$
 Identities = 9/24 (37%), Positives = 13/24 (54%)

Query: 208 FGELPLSLAACTKQWDVVSYLLEN 231
 FG+ L LA ++ VS LL +
 Sbjct: 171 FGQSALHLAIVHDDYETVSLLLNS 194

Score = 34 (15.8 bits), Expect = $3.6e-16$, Sum P(6) = $3.6e-16$
 Identities = 7/21 (33%), Positives = 11/21 (52%)

Query: 364 SPHRHRMVVLEPLNKLLQAKW 384
 +P M+ E + +LL KW
 Sbjct: 363 TPEHLDMIGSEVIQRLADKW 383

>GP:gi|2854148 (AF045639) contains similarity to ankyrin repeats
 [Caenorhabditis elegans]
 Length = 957

Score = 93 (43.2 bits), Expect = $7.6e-16$, Sum P(5) = $7.6e-16$
 Identities = 19/36 (52%), Positives = 25/36 (69%)

Query: 163 GHSALHTAIEKRSIQCVKLLVENGANVHARACGRFF 196
 G SALH+AI + V LL+ + A-V+ARACG FF
 Sbjct: 175 GQSALHLAIVHDDYETVSLLLNSKADVNARACGNFF 210

Score = 92 (42.7 bits), Expect = $7.6e-16$, Sum P(5) = $7.6e-16$
 Identities = 20/53 (37%), Positives = 31/53 (58%)

Query: 497 LLVSALVLGWLNLIIYYTRGFQHTGIYSVMIOKVILRLIRFLLIYLVFLFGFA 549
 L V AL W+ LL++ R + TG + MI +I D++RF +I +FL P+
 Sbjct: 503 LFPVLPGLSWIFLLFFARSAKLTGPFVQMIYSMIAGDMIRFAIISAIPLVSFS 555

Score = 57 (26.5 bits), Expect = $7.6e-16$, Sum P(5) = $7.6e-16$
 Identities = 10/24 (41%), Positives = 15/24 (62%)

Query: 207 YFGELPLSLAACTKQWDVVSYLLE 230
 Y+GE PL+ AAC D+ L++
 Sbjct: 229 YGGEYPLAFACFGNKKDIYDLLIQ 252

Score = 50 (23.2 bits), Expect = $7.6e-16$, Sum P(5) = $7.6e-16$
 Identities = 11/25 (44%), Positives = 15/25 (60%)

Query: 291 NLQDLTFLKLAKEGKIEIPRHILQ 315
 N TPL LA K G+ +IF +L+
 Sbjct: 297 NHAGFTPLTLATKLGRKQIFPEEMLE 321

Score = 44 (20.4 bits), Expect = $7.6e-16$, Sum P(5) = $7.6e-16$
 Identities = 10/24 (41%), Positives = 15/24 (62%)

Query: 242 DSQGNITVLHALVMISDNSAENIAL 265
 DS GNT+LH V+ -S + A+
 Sbjct: 261 DSFGNTILHMCVINYSSEMYSAV 284

Score = 37 (17.2 bits), Expect = $2.4e-05$, Sum P(4) = $2.4e-05$
 Identities = 9/24 (37%), Positives = 13/24 (54%)

Query: 208 FGELPLSLAACTKQWDVVSYLLEN 231
 FG+ L LA ++ VS LL +
 Sbjct: 174 FGQSALHLAIVHDDYETVSLLLNS 197

Score = 34 (15.8 bits), Expect = $4.1e-16$, Sum P(6) = $4.1e-16$
 Identities = 7/21 (33%), Positives = 11/21 (52%)

Query: 364 SPHRHRMVVLEPLNKLLQAKW 384
 +P M+ E + +LL KW
 Sbjct: 366 TPEHLDMIGSEVIQRLADKW 386

>GP:gi|3879753|gnl|PID|e1349345 (272514) Similarity to Human ankyrin
(SW:ANK1_HUMAN) (Caenorhabditis elegans)
Length = 519

Score = 73 (33.9 bits), Expect = 3.6e-11, Sum P(6) = 3.6e-11
Identities = 17/36 (47%), Positives = 19/36 (52%)

Query: 163 GHSALHIAIEKRSLSQCVKLLVENGANVHARACGRFF 198
G S L H A I L+ V L GA+VH R G FF
Sbjct: 186 GLSPLHQAIVNEDLENVYFLCRKGADVHQRCVGSFF 221

Score = 63 (29.3 bits), Expect = 3.6e-11, Sum P(6) = 3.6e-11
Identities = 12/17 (70%), Positives = 13/17 (76%)

Query: 207 YFGELPLSLAACTKQWD 223
Y+GE PLS AACT Q D
Sbjct: 252 YWGEYPLSFAACTNQVD 268

Score = 52 (24.1 bits), Expect = 3.6e-11, Sum P(6) = 3.6e-11
Identities = 13/27 (48%), Positives = 17/27 (62%)

Query: 289 IRNLQDLTFLKLAKEGKIEIPRHILQ 315
+RN LTPL LAA+ K I+ IL+
Sbjct: 315 VRNNLKLTPLALAARLAKKHIDILILE 341

Score = 51 (23.7 bits), Expect = 3.6e-11, Sum P(6) = 3.6e-11
Identities = 10/22 (45%), Positives = 12/22 (54%)

Query: 331 WCYGPFVRVSLYDLASVDSCEEN 352
W YGPV Y L VD+ E+
Sbjct: 348 WRYGPFVCKAYPLNDVDTINES 369

Score = 43 (20.0 bits), Expect = 3.6e-11, Sum P(6) = 3.6e-11
Identities = 8/13 (61%), Positives = 10/13 (76%)

Query: 242 DSQGNLVLHALVM 254
D+ GNTVLH V+
Sbjct: 284 DTNGNTVLHLTVI 296

Score = 37 (17.2 bits), Expect = 3.6e-11, Sum P(6) = 3.6e-11
Identities = 8/35 (22%), Positives = 16/35 (45%)

Query: 376 LNKLLQAKWDLIPKFFLNFCLNIYMFIF+VAY 410
+ ++L++KW+ K L IY +A+
Sbjct: 398 IEEVLESKWETFOKKQLFMSLAGYIYFLAVFYLA 432

>GP:gi|3287188|gnl|PID|e315126 (Y10601) ankyrin-like protein [Homo sapiens]
Length = 1119

Score = 71 (33.0 bits), Expect = 2.7e-08, Sum P(6) = 2.7e-08
Identities = 13/30 (43%), Positives = 20/30 (66%)

Query: 163 GHSALHIAIEKRSLSQCVKLLVENGANVHAR 192
G++ L H A+EK ++ VK L+ GAN + R
Sbjct: 98 GNTPLHCAVEKNQIESVKFLLSRGANPNLR 127

Score = 63 (29.3 bits), Expect = 2.7e-08, Sum P(6) = 2.7e-08
Identities = 10/30 (33%), Positives = 20/30 (66%)

Query: 501 ALVLGWLNLVLYYTRGFQHTCIYSVMIOKVI 530
A+ W+N L Y + F++ GI+ VM++ ++
Sbjct: 638 AVYFYWMNLYLYLQRPENCIGIFIVMLEVIL 667

Score = 59 (27.4 bits), Expect = $9.0e-07$, Sum P(6) = $9.0e-07$
Identities = 10/30 (33%), Positives = 19/30 (63%)

Query: 167 LHIAIEKRSIQCVKLLVENGANVHARACGR 196
LH+A++ L+ +K+ ++NGA + GR
Sbjct: 243 LHLAVQNGDLEMIMCLDNGAQIDPVEKGR 272

Score = 50 (23.2 bits), Expect = $2.7e-08$, Sum P(6) = $2.7e-08$
Identities = 10/26 (38%), Positives = 18/26 (69%)

Query: 291 NLQDLTFLKLAKEGKIEIFRHILQR 316
+L +TFL LAAG G ++ + -L++
Sbjct: 479 DLHGMTPLHLAAKNGHDKVQVQLLLKK 504

Score = 49 (22.8 bits), Expect = $2.7e-08$, Sum P(6) = $2.7e-08$
Identities = 10/26 (38%), Positives = 14/26 (53%)

Query: 209 GELPLSLAACTKQWDVVSYLENPHQ 234
G PL LA + W++V+ LL Q
Sbjct: 342 GRSPLILATASASWNIUNLLSKGAQ 367

Score = 48 (22.3 bits), Expect = $3.2e-05$, Sum P(5) = $3.2e-05$
Identities = 9/32 (28%), Positives = 20/32 (62%)

Query: 524 VMIOKVILRDLLRFLLIYLVFLFGFAVALVS 555
+++ +VIL+ LLR +++++ L F ++ -
Sbjct: 860 IVMLEVILKTLRSTVVFIPLLLAFGLSPYIL 891

Score = 41 (19.0 bits), Expect = $2.7e-08$, Sum P(6) = $2.7e-08$
Identities = 9/28 (32%), Positives = 15/28 (53%)

Query: 525 MIOKVILRDLLRFLLIYLVFLFGFAVAL 552
+I K +LR + P+ + L F F + L
Sbjct: 865 VILKTLRSTVVFIPLLLAFGLSPYIL 892

Score = 40 (18.6 bits), Expect = $2.9e-07$, Sum P(5) = $2.9e-07$
Identities = 13/50 (26%), Positives = 24/50 (48%)

Query: 620 MVLLLLLAYVLLTYILLNMLIALMSETVNSVATDSWSIWKLQKAVISLE 669
+V + LL L++ +LLN+ S ++ + TS + + S LE
Sbjct: 875 VVFIFPLLLAFGLSPYILNLDQPFSSPLLSIQTFSSMLGDINYRESFLE 924

Score = 40 (18.6 bits), Expect = $7.6e-05$, Sum P(5) = $7.6e-05$
Identities = 8/19 (42%), Positives = 12/19 (63%)

Query: 296 TPLKLAKEGKIEIFRHIL 314
TPL LA + G +B+ + L
Sbjct: 241 TPLHLAVQNGDLEMIMCL 259

Score = 39 (18.1 bits), Expect = $2.7e-08$, Sum P(6) = $2.7e-08$
Identities = 7/19 (36%), Positives = 14/19 (73%)

Query: 625 LLAYVLLTYILLNMLIAL 643
L+++ + I+L+N+LI L
Sbjct: 941 LVSTFIFVPIVLMNLLIGL 959

Score = 39 (18.1 bits), Expect = $6.8e-07$, Sum P(6) = $6.8e-07$
Identities = 9/36 (25%), Positives = 18/36 (50%)

Query: 293 QDLTFLKLAKEGKIEIFRHILQRFSGLSHLSRK 328
+ LT L + +IE+ H + +E+ + L+ F
Sbjct: 681 EPLTALNAMVQNVRIELNHPVCKEYLLMKWLAYGF 716

Exhibit D



Qualified Target Summary Sheet

| | |
|--|---|
| | Vanilloid Receptor Homologue (VR-2) |
| CFA Disease Area (s): | Pain |
| Druggable Target Class: | Calcium channel |
| MPI Gene Sequence Identifier: | Fih21e11 (Mine 18560) |
| Top Blast Hit: | Rat vanilloid receptor 1 (VR1) |
| Amino Acid Coding Region: | ORF: 361-2652 |
| CDNA Length: | 2806 bp |
| Source (Tissue / Cell Line): | First clone identified in an internal heart library |
| Novel / Unrecognized: | ? Unrecognized / Novel |
| % Novelty: | 66% novel across the complete cDNA.
Hits unannotated sequence in Non-Public Patent Data Base |
| Patent Status: | Filed Nov. 1, 1998 |
| Full Length Clone: | Yes |
| Expression Profiling Results: | Present in a sub-population of sensory neurons different from VR1.
Also present in sympathetic neurons. |
| Background: | The published vanilloid receptor (Caterina et. Al. Nature 389:816-24, 1997) responds to heat and capsaicin by activating Ca ⁺⁺ influx in sensory neurons (Tominaga et.al., Neuron 21: 531-43, 1998). Capsaicin also binds to this channel. |
| Hypothesis: | This channel may be responsible for hypersensitivity in chronic neuropathic pain and represents a unique target for pain. |
| Assay Type: | Cell-based assay |
| Reagents Needed: | Open reading frame will be cloned by Millennium into pCDNA 3.1 |
| Readout: | |
| Critical Experiments Necessary: | |

MPI Target Name:

Vanilloid Receptor Homologue (VR-2)

QT Nomination Date:

12/22/98

Action Taken:

Accepted QT (unrecognized) Pending full length cDNA

Date Accepted:

Bayer QT Leader:

Rory Curtis or Peter DiStefano

MPI QT Leader:


**BEFORE THE OFFICE OF ENROLLMENT AND DISCIPLINE
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